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Association of Indoor Air Pollution and Lifestyle with Lung Cancer in Osaka, Japan

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A hospital-based case-control study among non-smoking women was conducted to clarify risk factors in non-smoking females in Japan. Cases consisted of 144 non-smoking female lung cancer patients, and these were compared to 713 non-smoking female controls. The odds ratio (95% confidence interval) for use of wood or straw as cooking fuels when subjects were 30 years old was estimated as 1.77 (1.08 to 2.91). For those whose household members, other than husbands, had smoked, the odds ratio was estimated as 1.50 (1.01 to 2.32). For those whose mothers had smoked, the odds ratio was estimated as 1.28 (0.71 to 2.31). Use of heating appliances did not show an elevated risk. Some points to be noted in the study of low-risk agents for lung cancer are discussed.

In Japan, lung cancer was the second leading cause of cancer deaths for males and females in 1987.[1] In males, although smoking rates have been decreasing gradually since the 1970s, 61% of males smoked in 1988, which is considerably higher than in other developed countries. In females, however, smoking rates have been quite constant since the 1950s—only 13% of females smoked in 1988, which is low for a developed country. As a result, population attributable risks for lung cancer caused by smoking were estimated at 71% in males but only 26% in females.[2]

In the standard mortality ratio (SMR) analysis of the geographical distribution of lung cancer risks, a higher SMR was observed in coastal urban areas than in inland rural areas for males, but for females no such tendency was observed.[3] This indicates that occupational exposure and outdoor air pollution seem to have little influence as lung cancer risks for Japanese women. Therefore, it is necessary to investigate risk factors for females which might be related to daily lifestyle.

This study aims to clarify the risks of lung cancer caused by indoor air pollution among nonsmoking females by means of a hospital-based case-control study.

This work is part of a joint project of the research group for lung cancer prevention in Osaka. The members are listed in Appendix 1.

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MATERIAL AND METHODS

According to Osaka Cancer Registry, 2481 primary lung cancer (1977 males and 504 females) patients were diagnosed in Osaka Prefecture in 1985. Of these about one-quarter were registered from the top eight hospitals, which have special departments for lung cancer. These eight hospitals participated in a multi-centre, hospital-based case-control study with the support of the Osaka Anti-Lung Cancer Association.

Both cases and controls were collected from those newly admitted to the eight hospitals from 1 January, 1986 to 31 December 1988, and their ages ranged from 40 to 79 years at the time of hospitalization.

Of the above eight hospitals, all wards for lung cancer and one or two wards for other diseases were involved in this study. All newly-admitted patients, both males and females, in these wards were investigated by a self-administered questionnaire at the time of admission to the hospital. A uniform questionnaire was used in all hospitals, designed specifically for this study, which included questions about smoking habits, exposure to environmental tobacco smoke (ETS) and exposure to possible indoor air pollution. A total of 1079 lung cancer patients and 1369 patients of other diseases were investigated for males, and 295 lung cancer patients and 1073 patients of other disease for females. Males were not included in this analysis. For females, there were 55 current smokers, 64 ex-smokers, 156 nonsmokers and 20 patients with unknown smoking status for lung cancer patients, and

a corresponding 122, 92, 789 and 70 for patients of other diseases, respectively. Analysis was focused on 156 nonsmoking female lung cancer patients as cases and 589 female patients of other diseases as controls. No matching procedures were conducted between cases and controls. There were 12 cases and 58 controls excluded because of missing information on exposure. As a result, 144 cases and 531 controls comprised the total for this study.

Adjusted odds ratios were calculated by the Mantel-Haenszel method[7] using four levels of age categories at admission and two levels of education. Logistic regression analysis was performed including the variables which showed significant increase of risk in univariate analysis.[7]

RESULTS

All cases were microscopically confirmed, and had the following distribution—adenocarcinoma (78%), squamous cell carcinoma (8%), small cell carcinoma (5%), large cell carcinoma (5%), and other histological types (4%). Controls were diagnosed as having the following diseases: breast cancer (46%), stomach cancer (13%), other cancers (16%), benign neoplasms (8%), circulatory diseases (4%), respiratory diseases (3%), infectious disease (2%) and digestive diseases (2%).

Table 1 shows the distribution of age and educational level for cases and controls. The mean age at admission to hospitals was 60 for cases and 56 for controls. Higher education levels were observed for controls as compared to those for cases.

Table 2 shows adjusted odds ratios for lung cancer associated with use of wood or straw as cooking fuels according to the age at exposure. Significantly elevated risks were observed for subjects 30 years of age who had used wood or straw as cooking fuels. Use of these fuels at age 15, showed a slight increase or risk although it was not statistically significant. When the exposed were defined as those who used these fuels either at age 15 or age 30, the odds ratio was estimated as 1.28 with an 0.88–1.87 confidence interval.

In the calculation of the odds ratio, the use of heating appliances—kerosene, gas, coal, charcoal and wood stoves without chimneys were regarded as possible sources of exposure which could pollute indoor air with combustion products. Electric air conditioners, stoves with chimneys and electric stoves were not regarded as sources of exposure. There were no risk elevations observed for exposure at any age (Table 3). The charcoal foot warmer was popularly used until the 1960s, but is now rarely used in Japan. Again, risk elevation was not observed for exposure at any age (Table 4).

Odds ratios for lung cancer associated with ETS during childhood were shown by source of exposure (Table 5). A slight increase of risk was suggested for those with smoking mothers, although statistical significance was not observed.

As regards ETS in adulthood, an elevated risk was observed for those whose household members, other than husbands, had smoked (Table 6). Smokers among other household members consisted chiefly of the husband's father and sons.

Table 7 shows the results of logistic regression analysis, including the three variables in the model, which were suggested to raise the risk of lung cancer in univariate analysis. Use of wood or straw as cooking fuels at age 30 showed a risk 1.7 times higher, with statistical significance. The other two variables showed slightly increased risks, but were not statistically significant. The results from the same analysis, when breast cancer patients (controls) were excluded, showed similar results.

DISCUSSION

From the results of this study, the use of wood or straw as cooking fuels was suggested as a possible risk factor for current female lung cancer cases in Japan, despite

TABLE 1 *Distribution of age at admission and years of education for cases and controls*

Characteristics	Case		Control	
	N	%	N	%
Age at admission				
40–49	20	13.9	238	32.6
50–59	49	34.0	229	31.3
60–69	41	28.5	186	25.4
70–79	34	23.6	78	10.7
Years of education				
less than 9	69	47.9	229	31.3
10 or over	75	52.1	502	68.7

TABLE 2 *Odds ratios for lung cancer associated with the use of wood or straw as cooking fuels according to age at exposure*

	Case/Control	OR	(95% CI*)
Age 15			
No	59/361	1.00	
Yes	85/370	1.24	(0.86–1.81)
Age 30			
No	112/660	1.00	
Yes	32/71	1.89	(1.16–3.06)
Present			
No	144/731	1.00	
Yes	0/0	—	

*Confidence interval

TABLE 3 *Odds ratios for lung cancer associated with the use of heating equipment polluting room air with combustion products, according to age at exposure*

	Case/Control	OR	(95% CI*)
Age 15			
No	206/201	1.00	
Yes	104/530	1.01	(0.66–1.52)
Age 30			
No	51/294	1.00	
Yes	93/437	1.18	(0.81–1.72)
Present			
No	77/384	1.00	
Yes	67/327	1.11	(0.77–1.60)

*Confidence interval

its being an old practice. These types of cooking fuels were widespread until the 1960s even in suburban areas, but now very few people use them even in rural areas. Of those who used wood or straw at 30 years of age, 90% had also used these cooking fuels at 15 years of age. This indicates that those exposed at age 30 must have been exposed for a longer duration.

It is reported that use of cooking oil, especially rapeseed oil, increased the risk of lung cancer among Chinese women in Shanghai.[5] In the same report, however, the use of cooking fuel including coal, gas and wood did not show an elevated risk of lung cancer. In Hong Kong, the use of kerosene oil as cooking fuel appeared to increase the risk of lung cancer among Chinese women although the effects of these factors seemed to be limited.[6] It is also reported from Singapore that there was no difference of risk for lung cancer between those who used wood or charcoal and those who used petroleum or gas.[7] However, all these reports provided information concerning Chinese women, who practice different methods of cooking from Japanese women. Also, in these studies, the exposure from cooking fuels were defined as ever versus never or were based on only recent status, and the exposures variable may not correctly reflect the status of past exposure. In fact, when ever versus never analysis was used, the use of wood or straw as cooking fuels did not show a significant elevation of risk.

In the present study, no one was found who uses wood or straw as cooking fuels at present, so this does not constitute a factor for primary prevention in this country. However, this showed that the environmental exposures occurring 20 years ago could affect the incidence of lung cancer, which in turn means that some lifestyles widespread at present can be risk factors for lung cancer in the future although conventional epidemiological studies cannot reveal these factors at present.

It has been reported that some compounds found in wood smoke—benzo(a)pyrene and formaldehyde—are possible human carcinogens.[8] It has been shown that the aromatic fraction of wood smoke, which contains various polycyclic aromatic hydrocarbons has mutagenic activity.[9] Also, the polar fraction of organic extracts from emissions of wood combustion has been shown to have direct mutagenic activity.[10] It is reported that natural inhalation exposure to wood smoke increased the incidence of lung cancer in mice.[11]

The use of heating equipment for room air, including kerosene, gas, coal, charcoal and wood stoves without chimneys, did not show an elevated risk of lung cancer. Of these, charcoal and kerosene was most frequently used at age 15 and 30, respectively. Wood was used for heating fuel only for less than 5% of the population, therefore the risk due to wood stoves could not be evaluated. It is reported from Hong Kong that the use of kerosene stoves increased the risk in women.[6] In Japan, no increase of risk was observed for the use of kerosene stoves.[12]

ETS from the mother during childhood seemed to raise the risk but did not show statistical significance. It has been established that ETS for children increases the occurrence of lower respiratory illnesses, particu-

TABLE 4 *Odds ratios for lung cancer associated with the use of charcoal foot warmers for sleeping according to age at exposure*

	Case/Control	OR	(95% CI*)
Age 15			
No	91/470	1.00	
Yes	53/261	1.01	(0.69–1.48)
Age 30			
No	112/616	1.00	
Yes	32/115	1.05	(0.66–1.68)
Present			
No	143/725	1.00	
Yes	1/ 6	0.67	(0.09–5.12)

*Confidence interval

TABLE 5 *Odds ratios for lung cancer associated with environmental tobacco smoke during childhood by source of exposure*

	Case/Control	OR	(95% CI*)
Father smoked			
No	35/143	1.00	
Yes	109/588	0.79	(0.52–1.21)
Mother smoked			
No	127/668	1.00	
Yes	17/ 63	1.33	(0.74–2.37)
Other household members			
No	113/587	1.00	
Yes	31/144	1.18	(0.76–1.84)

*Confidence interval

TABLE 6. *Odds ratios for lung cancer associated with environmental tobacco smoke in adulthood by source of exposure*

	Case/Control	OR	(95% CI*)
Husband smoked			
No	64/336	1.00	
Yes	80/395	1.13	(0.78–1.63)
Other household members			
No	91/550	1.00	
Yes	53/181	1.57	(1.07–2.31)

*Confidence interval

larly early in life, and increases the frequency of chronic respiratory symptoms.[4,15] Its relation to lung cancer, however, has been less clear. It is reported that the odds ratio for lung cancer associated with exposure to a smoking mother for nonsmoking females was 1.7 in the U.S.[16] and 4.0 in Japan.[17]

Concerning ETS in adulthood, ETS from the husband did not show an elevated risk in this study. In Japan, a 50–100% increased risk for lung cancer associated with ETS from the husbands was reported[18,19] although some studies found no increase.[17] It is estimated from the meta-analysis dealing with two cohort studies and ten case-control studies that the increased risk of lung cancer by ETS from the husband would be 30%.[20] In the present study, ETS from household members other than the husband showed an increased risk of lung cancer. This is consistent with a report from Japan that ETS from the husband's father elevated the risk of lung cancer 3.2 times.[17]

Some methodological problems should be considered in this study. First, a substantial proportion of controls consisted of cancer patients, especially breast cancer. Although use of cancer controls has various merits and demerits,[21] it is obviously not appropriate to use controls from a single disease. When breast cancer was excluded from controls, the odds ratios for use of wood or straw as cooking fuels, ETS from the smoking mother, and ETS from household members other than the husband became 1.65, 162 and 1.47, respectively, which did not show substantial change.

Second, smoking status of the study subjects was investigated by self-administered questionnaires and no validation was conducted by other objective means, such as testing for cotinine in urine or carbon monoxide in expired breath. However, these methods cannot be applied to determine smoking status in the past only to recent smoking status. Further studies are needed in this area.

Third, the exact duration of intensity of exposure could not be investigated for use of cooking fuels and ETS from various sources of exposure. However, detailed information obtained from individual memory may not be reliable enough to conduct dose-response analysis.[22,23]

Fourth, no systematic review for histopathological diagnosis was carried out, but routine pathology reports were used. However, since all pathologists involved in the eight hospitals were specialists in lung cancer and had worked at least five years in this area, validity of these reports were thought to be quite high as far as the determination as to whether it was malignant or benign. The analysis in this study was not conducted by dividing lung cancer into histological types, and it is believed the effects of this on the results would be minimal.

There are some epidemiological points to be discussed in the study of low-risk agents. First, subjects were limited to low-risk individuals for lung cancer, which in this study were Japanese females who had never smoked. It is generally thought that focusing on low-risk individuals can strengthen the association between the disease and exposure,[24] making it easier to find possible associations, except when positive interactions exist.

Secondly, when we categorize the study subjects into exposed and non-exposed, it is important to pay attention to the timing between exposure and disease. According to the mechanisms of carcinogenesis, this appropriate time difference will vary. For example, if the agent in question acts mainly in the early stages of carcinogenesis, there should be a longer latency time between exposure and disease, but if the agent acts mainly in the later stages, the lag time between exposure and disease will be short. In this study, exposures were defined according to the patient's age, and were able to reveal the association between cooking fuel and lung cancer. However, if we use ordinary classifications, such as never-user versus ever-user, or present use, the association would not be seen.

Thirdly, even if we can use the appropriate classification of exposure, considering its timing in the occurrence of the disease, it is important that the population has the appropriate diversity in terms of exposure classification. In other words, there should be some proportion of people who will be classified as non-

TABLE 7. *Odds ratios estimated by logistic regression analysis. Adjusted for age at hospitalization.*

Variable	OR	(95% CI*)
Use of wood or straw at age 30	1.77	(1.08–2.91)
Other household members smoked in adulthood	1.50	(1.01–2.22)
Mother smoked in childhood	1.28	(0.71–2.31)

exposed together with people who will be classified as exposed. This is not always the case in the situation of cooking or heating practices, for which most people share a common tradition. In Japan, there have been drastic changes in lifestyle since World War II. Sanitary conditions in most houses were not very good in the 1950s, but have dramatically improved in the 1980s, and this can be regarded as an appropriate non-exposed situation. Mixed practices in cooking and heating were prevalent during this transitional period between the 1950s and 1980s, which provides a good opportunity to identify a low-risk agent for lung cancer associated with daily lifestyle.

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APPENDIX 1

Research group for lung cancer prevention in Osaka

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